REMARKS

Claims 1, 3, 4, 12, 14, and 15 have been amended to recite that the INGAP protein has the amino acid sequence shown in SEQ ID NO: 2. This is supported *inter alia* at column 5, lines 52-54.

Claim 7 is amended to recite that the polypeptide "is capable of stimulating beta cell regeneration in pancreatic ductal cells." This is supported at column 7, lines 32-33.

Claim 8 is amended to change its dependency in view of the amendment to claim 7 that removed antecedent basis for claim 8.

Claim 11 is amended to correct a typographical error and to make it dependent on claim 1. In addition, a former recitation of an inherent property has been changed to be a product-by-process limitation. This is supported by the claim as originally presented.

Claim 15 is amended to clarify the linguistic distinction between the fusion polypeptide and the second polypeptide which is a constituent part of the fusion polypeptide.

Claims 25 and 26 are amended to make explicit the product-by-process limitation and to clarify the recombinant genetic terminology, as requested by the examiner.

Claims 29, 31, 33-35, although not properly presented and entered previously, have been changed to spell out the underlying words for the acronym INGAP. These claims have also been amended to specify that the at least 15 amino acids are shown in the recited sequence.

It is respectfully submitted that no new matter has been added by these amendments.

Recapture Rule

Claims 29, 30, 33, and 34 are allegedly barred by the recapture rule. The Office Action asserts that these claims do not recite a function and that the prosecution history of claim 3 of the patent requires a function for these claims.

> The recapture rule bars the patentee from acquiring through reissue claims that are, in all aspects, of the same scope as, or are broader in scope than, those claims canceled from the original application to obtain a patent. *Ball Corp. v. U.S.*, 729 F.2d 1429 at 1436, 221 U.S.P.Q. 289 at 295 (Fed. Cir. 1984).
>
> The patentee is free to acquire, through reissue, claims that are narrower in scope in all aspects than claims canceled from the original application to obtain a patent. If the reissue claims are narrower than the claims canceled from the original application, yet broader than the original patent claims, reissue must be sought within 2 years after the grant of the original patent. *Ball*, 729 F.2d at 1436, 221 U.S.P.Q. at 295.

Thus, in a reissue filed within two years of the grant date, the recapture rule permits claims which, although broader than the patent claims, are narrower than the claims canceled from the original application. An expanded panel of the Board of Appeals has recently and exhaustively reviewed the legal standards governing recapture in *Ex parte Eggert*, Appeal No. 2001-0790 (2003). The Board of Appeals held that the recapture rule bars only recapture of subject matter which is the same as that surrendered during prosecution by amendment, cancellation, or argument. Subject matter which is broader than an issued patent claim but narrower than relinquished subject matter is permitted, if the reissue application is filed within two years of the grant date. Referring to a schematic drawing depicting two concentric circles with the area between them shaded (a donut) the Board identified the outer circle as representing the scope of the relinquished application claim and the inner circle as representing the scope of the granted patent claim. The Board explained:

> In our view, the surrendered subject matter is the outer circle of Drawing 1 because it is the subject matter appellants conceded was unpatentable. The subject matter of the shaded area was not subject to the administrative examination process as the examiner was never directly presented with a claim which fell within the scope of the shaded area. Thus, appellants have never conceded that a claim falling within the scope of the shaded area of Drawing 1 is unpatentable and therefore, in our view, such subject matter is not barred by the recapture rule.

The Board rejected the examiner's proposed *per se* rule of reissue recapture which would prevent patentees "from retreating from any claim limitation determined to have secured allowance of the original patent." *Ex parte Eggert* at page 5. Such a *per se* rule, the Board stated, would be contrary to the language of 35 U.S.C. § 251. *Ex parte Eggert* at page 5.

In the subject reissue application the Patent and Trademark Office cites the prosecution of claim 3 in the original application of the underlying patent. Claim 3 originally recited:

> 3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a mammalian INGAP protein.

The Patent and Trademark Office rejected claim 3 under 35 U.S.C. § 112, first paragraph, stating that "the disclosure is enabling only for claims limited to the INGAP protein and the INGAP peptide (amino acids 103-122 of SEQ ID NO:2) disclosed in the specification." Paper No. 11 at page 4. Applicants asserted that claim 3 was enabled for its full scope because "the specification teaches that fragments of INGAP are useful for raising antibodies and purifying them." Amendment filed April 10, 1997, at page 5. The Patent and Trademark Office later indicated that the rejection of claim 3 could be overcome by limiting the claim "to those fragments of INGAP having immunogenic activity." Paper No. 14 at page 6. Claim 3 was amended to recite

that "said polypeptide has immunogenic activity" (Amendment dated October 23, 1997) and subsequently allowed. Paper No. 16. The granted claim 3 recites:

> 3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said polypeptide has immunogenic activity.

The following table provides a side-by-side comparison of original application claim 3, issued claim 3, and rejected reissue claims 29, 30, 33, and 34. The element added during prosecution of the original application is shown in blue ("wherein said polypeptide has immunogenic activity"). The elements of granted claim 3 that are omitted in the reissue application claims are shown in red and blue ("of a naturally occurring mammalian" and "wherein said polypeptide has immunogenic activity"). The elements added to the reissue application claims relative to both original application claim 3 and issued claim 3 are shown in green ("shown in SEQ ID NO: 2, wherein said polypeptide is a portion" and "selected from amino acids #103 to #122 as shown in SEQ ID NO: 2").

ORIGINAL CLAIM 3	ISSUED CLAIM 3	REISSUE APPLICATION CLAIMS
3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian INGAP protein.	3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids **of a naturally occurring mammalian** islet neogenesis associated protein (INGAP protein), **wherein said polypeptide has immunogenic activity.**	29. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids **shown in SEQ ID NO: 2, wherein said polypeptide is a portion** of islet neogenesis associated protein (INGAP protein).
3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian INGAP protein.	3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids **of a naturally occurring mammalian** islet neogenesis associated protein (INGAP protein), **wherein said polypeptide has immunogenic activity.**	30. The preparation of claim 29 wherein the polypeptide comprises a sequence of at least 15 consecutive amino acids **selected from amino acids #103 to #122 as shown in SEQ ID NO: 2.**
3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian INGAP protein.	3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids **of a naturally occurring mammalian** islet neogenesis associated protein (INGAP protein), **wherein said polypeptide has immunogenic activity.**	33. A preparation of a polypeptide which **consists of a portion of** islet neogenesis associated protein (INGAP protein) of at least 15 consecutive amino acids **shown in SEQ ID NO: 2.**
3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian INGAP protein.	3. A preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids **of a naturally occurring mammalian** islet neogenesis associated protein (INGAP protein), **wherein said polypeptide has immunogenic activity.**	34. The preparation of claim 33 wherein the polypeptide **consists of a portion of** islet neogenesis associated protein (INGAP protein) of at least 15 consecutive amino acids **selected from amino acids #103 to #122 as shown in SEQ ID NO: 2.**

Each of reissue application claims 29, 30, 33, and 34 recites that the claimed polypeptide has "at least 15 consecutive amino acids shown in SEQ ID NO:2." Original application claim 3 contained no sequence recitation. Thus, each of the rejected reissue application claims is narrower than claim 3 as originally presented in the original application. According to *Ball, Eggert,* and 35 U.S.C. § 251, the patentee is free to acquire through reissue such claims as claims 29, 30, 33, and 34 that are narrower than original application claims.

Withdrawal of this rejection is therefore respectfully requested.

The Rejection of Claims 7, 8, 15, 17, 18, 25, 26, and 29-36 Under 35 U.S.C. § 112, second paragraph

Claims 7 and 17 are allegedly unclear in the use of the term "biological activity." Claim 7 has been amended to recite "stimulation of beta cell regeneration in pancreatic ductal cells." Claim 17 has been cancelled.

Claim 11 has been amended to correct a typographical error of the word "neogenesis."

Claim 15 was allegedly unclear in describing which polypeptide is responsible for the biological activity. Claim 15 has been amended to specify that the fusion polypeptide has the recited biological activity.

Claims 25 and 26 were objected to for their use of the term "vector." The claims have been amended as suggested by the examiner.

Claims 29-36 have been amended to define the acronym INGAP in each claim. These claims are also allegedly awkward. Applicants have amended claims 29, 31, 33 and 35 to specify that the at least 15 consecutive amino acids are shown in SEQ ID NO:2.

Applicants do not concede that the claims were previously unclear or indefinite, but amend the claims to expedite prosecution.

The Rejection of Claims 1, 3, 5-8, 11, 12, 14-18, 21-29 and 33 Under 35 U.S.C. § 112, first paragraph

Certain claims are rejected as lacking [adequate] written description for failing to define a protein by both structure and function. This rejection is respectfully traversed.

Claims 1, 3, 12, 14, 15 have been amended to recite that "the INGAP protein has the amino acid sequence shown in SEQ ID NO:2." Thus, each of these claims recites a complete protein sequence. It is respectfully submitted that a structure is all that is required to adequately describe the claimed subject matter. Although the specification discloses a function for the INGAP protein (note the absence of any rejections for lack of utility) a function need not be recited in the claims. The Patent and Trademark Office has provided no legal support or reasoning that identifies the source of the alleged requirement for defining claimed subject matter by structure and function. Claims 5-8, 11, 16, 21-28 each refer back to an earlier claim which has been amended to recite a complete structure. Thus, these claims are also supported by an adequate description. Claims 17-18 have been canceled. Claims 29 and 33 recited SEQ ID NO:2 as presented. It is respectfully submitted that these claims, like amended claims 1, 3, 12, 14 and 15 which recite a complete structure are sufficiently described in the specification. Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 1, 3, 8, 12, 14, 17, 18, 21, 25, 26, 27, and 28 Under 35 U.S.C. § 102(a)

Certain claims are rejected as anticipated by Watanabe *et al.* This rejection is respectfully traversed.

To reject a claim as anticipated, each and every element as set forth in the claim must be either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d (BNA) 1051, 1053 (Fed. Cir. 1987).

Each of claims 1, 3, 8, 12, 14, 17, 18, 21, 25, 26, 27, and 28 requires at least 15 consecutive amino acids shown in SEQ ID NO: 2.

Watanabe is cited as teaching rat Reg protein. The amino acid sequence of rat Reg protein is shown in SEQ ID NO: 7 of the subject application. It is compared to the amino acid sequence of INGAP protein in Fig. 2 of the subject application. It is respectfully submitted that rat Reg protein does not comprise at least 15 consecutive amino acids of SEQ ID NO:2 as required by each of the rejected claims.[1]

Because Watanabe does not teach, either expressly or inherently, a protein or polypeptide that has at least 15 consecutive amino acids shown in SEQ ID NO: 2, it does not describe each and every element as set forth in the rejected claims. Absent such a description in Watanabe, the rejection for anticipation cannot be maintained. Withdrawal of this rejection is therefore respectfully requested.

The Rejection of Claims 1, 3, 7, 8 12, 14, 17, 18, 21, 25, 26, 27, and 28 Under 35 U.S.C. § 102(b)

Certain claims are rejected as anticipated by Pittenger (1992). This rejection is respectfully traversed.

[1] Upon visual inspection, no stretches of 15 consecutive amino acid identity were observed. The largest stretch of identity noted was 7 amino acids in length. The Patent and Trademark Office is invited to make its own machine-comparison rather than relying on the undersigned attorney's visual inspection

To reject a claim as anticipated, each and every element as set forth in the claim must be either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California,* 814 F.2d 628, 631, 2 U.S.P.Q.2d (BNA) 1051, 1053 (Fed. Cir. 1987). Moreover, an anticipatory reference must enable one of ordinary skill in the art to practice the invention. *In re LeGrice,* 301 F.2d 929, 133 U.S.P.Q. 365 (C.C.P.A. 1962).

Pittenger is cited as teaching ilotropin. Pittenger teaches a preparation of ilotropin which is not a pure protein. Pittenger teaches that two protein bands of 30-40 KDa among many on an SDS/polyacrylamide gel are enriched in a wrapped pancreas cytosol extract. Page 126, first full paragraph. Pittenger also reports that ilotropin bioactivity eluted from a Superose-12® FPLC column in two peaks between molecular weight markers of 24 KDa and 66 KDa.[2] Page 126, last paragraph. Pittenger does not, however, indicate that the proteins eluting in the two peaks between molecular weight markers for 24 KDa and 66 6KDa represent purified proteins. In fact, Figure 1 indicates the presence of multiple bands in that molecular weight range in the "partially purified cytosol extract." Moreover, Pittenger states in the article's summary that the authors were still trying to further purify ilotropin to homogeneity: "Current studies of ilotropin include further purification to homogeneity...." Page 129, last paragraph. Even more telling is the discussion appended to the end of Pittenger. When asked how pure the material was, Pittenger replied, "We have it down, probably, to five, maybe, ten spots, something that we can pursue."

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[2] The Office Action asserts that ilotropin was conjugated to a solid support because it was bound and eluted from a Superose-12® FLPC column. Page 5, lines 5-9. Reversible binding to a column, however, is not the same as conjugation to a solid support. Conjugation involves a covalent bond. See the subject application at column 10, line 35.

Page 131, paragraph 2. Thus, Pittenger specifically concedes that the preparation taught in its 1992 paper was not remotely close to homogeneous.

Claims 1, 11, 25, and 27 require substantial freedom from other mammalian proteins. As discussed above, Pittenger does not teach such a preparation. Claims 21 and 22 require an increased level of purity: "free of other mammalian proteins" and "free from other proteins of the mammal," respectively. Perforce Pittenger does not teach such increased purity levels.

There is no evidence that the ilotropin taught by Pittenger is the same as INGAP of SEQ ID NO: 2. The limited evidence available suggests that INGAP and ilotropin are different, based on molecular weight. The calculated molecular weight of INGAP of SEQ ID NO:2 is approximately 18 KDa, whereas Pittenger teaches a molecular weight of 30-40 KDa. Thus, Pittenger neither expressly nor inherently teaches each and every element of the claimed invention.

Even if *arguendo* Pittenger were deemed to describe the same protein as INGAP, it does not enable one of skill in the art to make the INGAP compositions as claimed. Pittenger does not teach a successful method of purifying INGAP. Pittenger does not teach an accurate molecular weight for INGAP. One of ordinary skill in the art would not have been able to make INGAP compositions as claimed based on Pittenger's description without resorting to undue experimentation.

Claims 3, 6, 7, 8, 12, 14, 17, 18, 21, 22, 26, and 28 each require a particular amino acid sequence. There is no evidence that Pittenger's ilotropin protein has such a sequence. Based on its molecular weight, it appears that ilotropin is a different protein and thus likely to have a different amino acid sequence.

This rejection should be withdrawn with regard to all claims because the cited document does not teach, either expressly or inherently, the claimed compositions.

Form 1449

Applicants filed an Information Disclosure Statement with the reissue application containing two pages of form 1449. Applicants received back only page 1 of 2 with the examiners initials upon it. A fresh copy of page 2 of 2 is enclosed in case this page became lost before reaching the examiner.

Surrender of Patent

Applicants surrender the original patent grant contingent upon its reissue.

Respectfully submitted,

Date: December 17, 2003

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Enclosures: Original patent grant
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